WO 2005/007889

5

- 46 -

CLAIMS

- 1. A method of diagnosing CRC or a predisposition for developing CRC in a subject, comprising determining a level of expression of FGF18 in a patient-derived biological sample, wherein an increase of said level as compared to a normal control level of said gene indicates that said subject suffers from or is at risk for developing CRC.
 - 2. The method of claim 1, wherein said determined expression level is at least 10% greater than said normal control level.
- The method of claim 1, wherein the expression level is determined by any one method selected from group consisting of:
 - (a) detecting mRNA of FGF18,
 - (b) detecting a protein encoded by FGF18, and
 - (c) detecting a biological activity of a protein encoded by FGF18,
- 15 4. The method of claim 1, wherein said level of expression is determined by detecting hybridization of an FGF18 probe to a gene transcript of said patient-derived biological sample.
 - 5. The method of claim 4, wherein said hybridization step is carried out on a DNA array.
- 20 6. The method of claim 1, wherein said biological sample comprises an epithelial cell.
 - 7. The method of claim 1, wherein said biological sample comprises a CRC cell.
 - 8. The method of claim 4, wherein said biological sample comprises an epithelial cell from a CRC.
- 9. A method of screening for a compound for treating or preventing CRC, said method comprising the steps of:
 - a) contacting a test compound with a polypeptide encoded by a nucleic acid of FGF18;
 - b) detecting the binding activity between the polypeptide and the test compound; and
- 30 c) selecting a compound that binds to the polypeptide.
 - 10. A method of screening for a compound for treating or preventing CRC, said method comprising the steps of:

WO 2005/007889 PCT/JP2004/010442

- 47 -

- a) contacting a candidate compound with a cell expressing FGF18, and
- b) selecting a compound that reduces the expression level of FGF18.
- 11. The method of claim 10, wherein said cell comprises a colorectal cancer cell.
- 12. A method of screening for a compound for treating or preventing CRC, said method comprising the steps of:

5

10

15

20

25

30

- a) contacting a test compound with a polypeptide encoded by a nucleic acid of FGF18:
- b) detecting the biological activity of the polypeptide of step (a); and
- c) selecting a compound that suppresses the biological activity of the polypeptide encoded by a nucleic acid of FGF18 in comparison with the biological activity detected in the absence of the test compound.
- 13. The method of claim 12, wherein the biological activity of the polypeptide is cell proliferative activity.
- 14. A method of screening for compound for treating or preventing CRC, said method comprising the steps of:
 - a) contacting a candidate compound with a cell into which a vector comprising the transcriptional regulatory region of FGF18 and a reporter gene that is expressed under the control of the transcriptional regulatory region has been introduced
 - b) measuring the activity or expression of said reporter gene; and
- selecting a compound that reduces the activity or expression level of said reporter gene, as compared to a control.
 - 15. The method of claim14, wherein the transcriptional regulatory region comprises the ß-catenin/Tcf4 binding motief in the transcriptional regulatory region of FGF18.
- 16. The method of claim 15, wherein said binding motif consists of nucleotide sequence set forth in SEQ ID NO: 24.
 - 17. A method of screening for compound for treating or preventing CRC, said method comprising the steps of:
 - a) contacting a DNA comprising a β-catenin/Tcf4 binding motif in the transcriptional regulatory region of FGF18 with a β-catenin/Tcf4 complex in the presence or absence of a candidate compound;
 - b) detecting the binding of the DNA and the \(\beta\)-catenin/Tcf4 complex; and

WO 2005/007889 PCT/JP2004/010442

- 48 -

- c) selecting a compound that inhibits the binding of the B-catenin/Tcf4 complex with the DNA,, as compared to a control.
- 18. The method of claim 17, wherein said binding motif consists of SEQ ID NO: 24.
- A kit comprising a detection reagent which binds to nucleic acid sequence or polypeptide of FGF18.

5

20

- 20. A method of treating or preventing CRC in a subject comprising administering to said subject an antisense composition, said composition comprising a nucleotide sequence complementary to a coding sequence of FGF18.
- 21. A method of treating or preventing CRC in a subject comprising administering to said subject a siRNA composition, wherein said composition reduces the expression of a nucleic acid sequence of FGF18.
 - 22. The method of claim 21, wherein the siRNA comprises a sense strand comprising the nucleotide sequence of SEQ ID NO: 21.
- 23. A method for treating or preventing CRC in a subject comprising the step of administering to said subject a pharmaceutically effective amount of an antibody or fragment thereof that binds to a protein encoded by nucleic acid of FGF18.
 - 24. A method of treating or preventing CRC in a subject comprising administering to said subject a vaccine comprising a polypeptide encoded by a nucleic acid of FGF18 or an immunologically active fragment of said polypeptide, or a polynucleotide encoding the polypeptide.
 - 25. A method for treating or preventing CRC in a subject, said method comprising the step of administering a compound that is obtained by the method according to any one of claims 9-18.
- A composition for treating or preventing CRC, said composition comprising a
 pharmaceutically effective amount of an antisense polynucleotide or small interfering RNA against a polynucleotide of FGF18.
 - 27. The composition of claim 26, wherein the siRNA comprises a sense strand comprising the nucleotide sequence of SEQ ID NO: 21.
- 28. A composition for treating or preventing CRC, said composition comprising a

 pharmaceutically effective amount of an antibody or fragment thereof that binds to a
 protein encoded by nucleic acid of FGF18.

WO 2005/007889 PCT/JP2004/010442

- 49 -

29. A composition for treating or preventing CRC, said composition comprising a pharmaceutically effective amount of the compound selected by the method of any one of claims 9-18 as an active ingredient, and a pharmaceutically acceptable carrier.